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Regiospecific Syntheses of All Isomeric Nitrofluorenones and Nitrofluorenes by Transition Metal Catalyzed Cross Coupling Reactions

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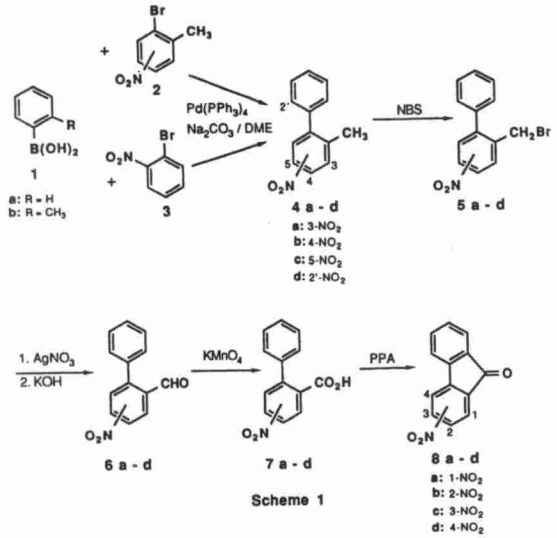
INTRODUCTION

Nitro polycyclic aromatic hydrocarbons (Nitro-PAH) are environmental pollutants which have been increasingly detected in urban ambient air particulates, diesel exhaust emissions, fly ash, photocopier fluids, and cigarette smoke.[2] The accumulating evidence of the wide environmental distribution of nitro polycyclic aromatic hydrocarbons (PAH) and the discovery, in 1980, of their potent direct acting mutagenicity has prompted increased activity in the detection, identification, and quantitation of these toxic materials.[2] Of the over 200 nitro PAH which have been recognized, the nitrofluorenes constitute one of the most potent mutagenic classes whose identification and metabolism, currently under intense study,[3] require pure analytical standards.

Available methods for the syntheses of nitrofluorenes are based on classical electrophilic nitration which provides the 2-nitro isomer in good yield but which, depending on conditions, leads to mixtures of isomeric mononitro products (including 4-nitrofluorene) requiring tedious separation and purification procedures.[2] In order to provide high purity samples obligatory for analytical and biological work, we have developed and report herein a new regiospecific and convenient route to all isomeric nitrofluorenones and nitrofluorenes which is based on the Pd(0)-catalyzed cross coupling methodology for biaryls under investigation in our laboratory.[4]

RESULTS AND DISCUSSION

Treatment of phenyl boronic acid **1a** with the bromo nitrotoluenes **2a-c** under the modified Suzuki conditions[4c] afforded the methyl nitrobiphenyls **4a-c** in high yield (**Scheme 1**). 2-methyl-2'-nitrobiphenyl **4d** was similarly prepared by coupling the 2-methylphenylboronic acid **1b** with 1-bromo-2-nitrobenzene **3**. Reaction of **4a-d** with NBS yielded the benzyl bromides **5a-d** which, when subjected to a standard two stage oxidation procedure[5] using $AgNO_3$/KOH and $KMnO_4$, provided the carboxylic acids **7a-d**. PPA cyclization led smoothly to the nitrofluorenones **8a-d**. Et_3SiH/TFA reduction[6] was found to be unsatisfactory for all except the 4-nitrofluorenone **8d** which led to the corresponding nitrofluorene **10d** in modest (39%) yield.[7]

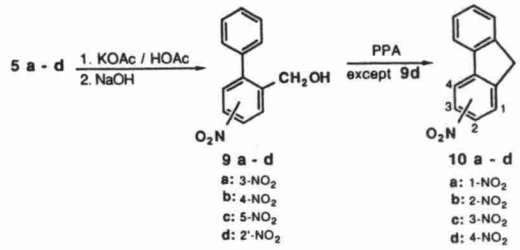


Scheme 1

To circumvent the reduction problem, the benzyl bromides **5a-d** (**Scheme 2**) were converted into the carbinols **9a-d** via the respective unisolated acetate intermediates. Direct cyclization of

9a-c with PPA provided the nitrofluorenes **10a-c** in excellent yields while **9d** led only to polymeric material. Thus although the acylium ion Friedel-Crafts cyclization of **7d** occurs readily to give the fluorenone **8d**, the carbenium ion derived from the corresponding carbinol **9d** undoubtedly undergoes more facile intermolecular electrophilic substitution rather than intramolecular reaction into the deactivated nitrobenzene ring.

In summary, this work provides easy access to 1-, 2-, 3-, and 4-nitro-fluorenones **8a-d** (31→ 46%) and -fluorenes **10a-d** in (12 → 67%) overall yields. Although the route to **10d** somewhat inefficient, all nitro-fluorenone and -fluorene products are obtained as single isomers whose ultra purification is not frought with the difficulties of separation of trace quantities of contaminating isomers.



Scheme 2

MATERIALS AND METHODS

Melting points were determined on a Büchi SMP-20 melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 983 infrared spectrophotometer. ^1H NMR spectra were recorded on AC-200 or AM 250 spectrometers using tetramethylsilane as internal standard. Mass spectral measurements were performed by Dr. R. Smith, McMaster University, Hamilton, Ontario, Canada.

All bromonitrotoluenes and phenylboronic acid were obtained from Aldrich Chemical Co. while 1-bromo-2-nitrobenzene and 2-bromotoluene were purchased from Lancaster Synthesis Ltd.

Polyphosphoric acid (PPA) (practical grade) was purchased from Manufacturing Chemists, Inc. Dimethoxyethane (DME) was purified by distillation over CaH_2 under nitrogen. Unless otherwise indicated, standard workup is equivalent to the following operation: the reaction mixture was treated with water or saturated aq. NaCl and extracted with $CHCl_3$; the organic extract was dried with $MgSO_4$ and evaporated to dryness in vacuo.

Preparation of Methyl Nitrobiphenyls 4a-d and 6b; General Procedure:

2-Methyl-3-nitrobiphenyl (4a). To a solution of $Pd(PPh_3)_4$ (1.049 g, 0.91 mmol) in DME was added a solution of 2-bromo-6-nitrotoluene (4.054 g, 18.77 mmol) in DME (60 mL) and the mixture was stirred for 15 min under nitrogen. A solution of phenylboronic acid (3.451 g, 28.30 mmol) in EtOH (15 mL) was added, the mixture was stirred for 10 min and then treated with aqueous Na_2CO_3 (2M, 80 mL). The resulting solution was refluxed for 20 h, cooled, and the organic layer was separated. Standard workup followed by chromatography (hexane:benzene, 5:1) afforded 3.848 g (96%) of **4a**, mp 72-73°C (Et_2O:hexane) (Lit.[8] mp 72.5-73°C); IR($CHCl_3$) ν(max) 1528, 1353 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3H, CH_3), 7.26-7.49 (m, 7H, ArH), 7.79 (d, J = 7.0 Hz, 1H, ArH); MS m/e (rel intensity) 213 (M, 68), 196 (100), 165 (78), 152 (43).

According to the above procedure, the following compounds were prepared:

2-Methyl-4-nitrobiphenyl (4b). 2-Bromo-5-nitrotoluene (5.016 g, 23.22 mmol), phenylboronic acid (4.232 g, 34.71 mmol), $Pd(PPh_3)_4$ (1.315 g, 1.14 mmol); yield: 93%; mp 55-56°C (Et_2O:hexane) (Lit.[9] mp 55-56°C); IR (Nujol) ν(max) 1515, 1344 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (s, 3H, CH_3), 7.25-7.50 (m, 6H, ArH), 8.08 (dd, J = 8.3, 2.2 Hz, 1H, ArH), 8.14 (d, J = 2.2 Hz, 1H, ArH); MS m/e (rel intensity) 213 (M, 100), 165 (40), 152 (34).

2-Methyl-5-nitrobiphenyl (4c). 2-Bromo-4-nitrotoluene (3.956 g, 18.30 mmol), phenylboronic acid (3.360 g, 27.56 mmol), $Pd(PPh_3)_4$ (1.067 g, 0.92 mmol); yield: 99%; mp 76-77°C (Et_2O:hexane) (Lit.[10] mp 75.5 - 76.5°C); IR ($CHCl_3$) ν(max) 1519, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (s, 3H, CH_3), 7.26-7.48 (m, 6H, ArH), 8.08-8.11 (m, 2H, ArH); MS m/e (rel intensity) 213 (M, 100), 165 (59), 152 (57).

2-Methyl-2'-nitrobiphenyl (4d). 1-Bromo-2-nitrobenzene (1.010 g, 5 mmol), (2-methylphenyl)boronic acid[11] (0.952 g, 7 mmol) (prepared from 2-bromotoluene via metal-halogen exchange with n-butyllithium and quenched with trimethyl borate and acidic workup), $Pd(PPh_3)_4$ (0.289 g, 0.25 mmol); yield: 96%; mp 63.5-64.5°C (pentane) (Lit.[11] mp 63-64°C); IR ($CHCl_3$) ν(max) 1522, 1351 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10 (s, 3H, CH_3), 7.08-7.35 (m, 5H, ArH), 7.47-7.67 (m, 2H, ArH), 7.96-8.01 (dd, J = 1.4, 8.0 Hz, 1H, ArH); MS m/e (rel intensity) 213 (M, 31), 196 (58), 183 (63), 165 (100), 152 (28).

2-Formyl-4-Nitrobiphenyl (6b). 2-Bromo-5-nitro-benzaldehyde (1.150 g, 5.00 mmol), phenylboronic acid (0.854 g, 7.00 mmol), $Pd(PPh_3)_4$ (0.231 g, 0.20 mmol); yield: 95%; mp 74-74.5°C (hexane); IR ($CHCl_3$) ν(max) 1691, 1525; 1347 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40-7.69 (m, 6H, ArH), 8.45-8.50 (dd, J = 2.5, 8.4 Hz, 1H, ArH), 8.85 (d, J = 2.4 Hz, 1H, ArH), 10.00 (s, 1H, CHO); MS m/e (rel intensity) 227 (M, 85), 180 (46), 152 (100); HRMS Calcd: 227.0583. Found: 227.0579.

Preparation of Bromomethyl Nitrobiphenyls 5a-d; General Procedure:

2-Bromomethyl-3-Nitrobiphenyl (5a). A solution of 2-methyl-3-nitrobiphenyl (0.382 g, 1.79 mmol), N-bromosuccinimide (0.333 g, 1.87 mmol), and a few crystals of benzoyl peroxide in CCl_4 (15 mL) was refluxed (36 h), cooled, treated with benzene (50 mL), and the whole was filtered and evaporated to dryness in vacuo. The crude material was chromatographed (hexane:EtOAc, 20:1) to give 0.490 g (94%) of **5a**, mp 72.5-73°C (Et_2O:hexane); IR (Nujol) ν(max) 1516, 1354, 1223 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.71 (s, 2H, CH_2), 7.54-7.38 (m, 7H, ArH), 7.96-7.88 (m, 1H, ArH); MS m/e (rel intensity) 293 (M + 1, 2), 291 (M - 1, 2), 212 (61), 166 (63), 165 (100); HRMS Calcd: 290.9895. Found: 290.9892.

Using the above procedure, the following compounds were prepared:

2-Bromomethyl-4-Nitrobiphenyl (5b). 2-Methyl-4-nitrobiphenyl (4.313 g, 20.23 mmol), NBS (3.788 g, 21.28 mmol); yield: 73%; mp 88-88.5°C (Et_2O:hexane); IR (Nujol) ν(max) 1505, 1347 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.46 (s, 2H, CH_2), 7.40-7.55 (m, 6H, ArH), 8.18 (dd, J = 2.4, 8.5 Hz, 1H, ArH), 8.41 (d, J = 2.4 Hz, 1H, ArH); MS m/e (rel intensity) 293 (M + 1, 16), 291 (M - 1, 16), 212 (63), 166 (100), 165 (74); HRMS Calcd: 290.9895. Found: 290.9889.

2-Bromomethyl-5-Nitrobiphenyl (5c). 2-Methyl-5-nitrobiphenyl (0.416 g, 1.95 mmol), NBS (0.365 g, 2.05 mmol); yield: 76%; mp 59-59.5°C (Et_2O:hexane); IR (Nujol) ν(max) 1516, 1354 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.44 (s, 2H), 7.4-7.5 (m, 5H, ArH), 7.70 (d, J = 8.5 Hz, 1H, ArH), 8.14 (d, J = 2.4 Hz, 1H, ArH), 8.20 (dd, J = 2.4, 8.5 Hz, 1H, ArH); MS m/e (rel intensity) 293 (M + 1, 7), 291 (M - 1, 7), 212 (59), 166 (78), 165 (100); HRMS Calcd: 290.9895. Found: 290.9881.

2-Bromomethyl-2'-Nitrobiphenyl (5d). 2-Methyl-2'-nitrobiphenyl (0.411 g, 1.93 mmol). NBS (0.358 g, 2.01 mmol); yield: 75%; mp 83-83.5°C (Et_2O:hexane) (Lit.[12] mp 77-79°C); IR (Nujol) ν(max) 1517, 1354 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.17 (d, J = 10.4 Hz, 1H, CH_2Br), 4.41 (d, J = 10.4 Hz, 1H, CH_2Br), 7.10 (dd, J = 1.3, 7.5 Hz, 1H, ArH), 7.20-7.70 (m, 6H, ArH), 8.04 (dd, J = 1.2, 8.1 Hz, 1H, ArH); MS m/e (rel intensity) 293 (M + 1, 1), 291 (M - 1, 1), 212 (40), 166 (100), 165 (65).

Preparation of Formyl Nitrobiphenyls 6a-d; General Procedure:

2-Formyl-3-Nitrobiphenyl (6a). To a solution of 2-bromomethyl-3-nitrobiphenyl **(5a)** (1.069 g, 3.66 mmol) in dioxane (50 mL) was added a solution of silver nitrate (2.555 g, 15.04 mmol) in water (5 mL) and the whole was stirred at room temperature for 18 h. The reaction mixture was filtered, the residue was washed with EtOAc, the filtrate was treated with water, and the organic layer was separated. The aqueous layer was extracted with EtOAc (2 x 70 mL) and the combined organic layer was subjected to standard work up. Chromatography (hexane-EtOAc, 15:1 → 10:1) afforded 0.773 g (77%) of **2-nitratomethyl-3-nitrobiphenyl** which was used without further purification. To a solution of this material (0.673 g, 2.46 mmol) in dioxane (40 mL) was added a solution of KOH (2.257 g, 40.20 mmol) in water. The mixture was stirred at room temperature for 20h, poured into water (50 mL), and the resulting solution was treated with saturated aq NaCl. The whole was extracted with CH_2Cl_2 (3 x 50 mL) and the extract was dried ($MgSO_4$) and evaporated in vacuo. Chromatography (hexane:EtOAc, 10:1) furnished 0.518 g (93%) of **6a**, mp 77.5-78°C (Et_2O:hexane); IR (Nujol) ν(max) 1705, 1528, 1345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.29-7.35 (m, 2H, ArH), 7.43-7.50 (m, 3H, ArH), 7.65-7.74 (m, 2H, ArH), 7.88-7.95 (m, 1H, ArH), 10.20 (s, 1H, CHO); MS m/e (rel intensity) 227 (M, 1), 152 (100); HRMS Calcd: 227.0583. Found: 227.0586.

2-Formyl-4-Nitrobiphenyl (6b). 2-Bromomethyl-4-nitrobiphenyl (1.847 g, 6.32 mmol); $AgNO_3$ (4.401 g, 25.91 mmol); KOH (5.419 g, 96.59 mmol); yield: 82%. This compound was shown (mp, ^1H NMR) to be identical with a sample prepared by the cross coupling procedure described above.

2-Formyl-5-Nitrobiphenyl (6c). 2-Bromomethyl-5-nitrobiphenyl (0.227 g, 0.78 mmol), $AgNO_3$ (0.552 g, 3.25 mmol), KOH (0.630 g, 11.23 mmol); yield: 71%; mp 100-107°C (Et_2O:hexane); IR (Nujol) ν(max) 1686, 1520, 1343 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35-7.56 (m, 5H, ArH), 8.17 (d, J = 8.4 Hz, 1H, ArH), 8.25-8.35 (m, 2H, ArH), 10.0 (s, 1H, CHO); MS m/e (rel intensity) 227 (M, 92), 226 (M - 1, 78), 180 (30), 152 (100); HRMS Calcd: 227.0583. Found: 227.0586.

2-Formyl-2'-Nitrobiphenyl (6d). 2-Bromomethyl-2'-nitrobiphenyl (0.372 g, 1.27 mmol), $AgNO_3$ (0.886 g, 5.21 mmol), KOH (1.128 g, 20.11 mmol); yield: 69%; mp 72-73°C (Et_2O:hexane); IR (Nujol) ν(max) 1690, 1520, 1268, 1246 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.2-7.8 (m, 6H, ArH), 7.9-8.15 (m, 2H), 9.86 (s, 1H, CHO); MS m/e (rel intensity) 227 (M, 1), 181 (100), 152 (100); MS(CI) m/e 245 ($M^+ + NH_4$).

Preparation of Carboxy Nitrobiphenyls 7a-d; General Procedure:

2-Carboxy-3-Nitrobiphenyl (7a). To a solution of 2-formyl-3-nitrobiphenyl **(6a)** (0.4754 g, 2.09 mmol) in acetone (20 mL) was added a solution of $KMnO_4$ (0.498 g, 3.15 mmol) in water (25 mL) and the mixture was stirred at room temperature for 4 h. It was treated with 5% aq Na_2SO_3 (50 mL), acidified (conc HCl), and the whole was extracted with $CHCl_3$ (3 x 50 mL). The organic extract was washed with water (50 mL) and extracted with 10% aq NaOH (2 x 30 mL). The alkaline extract was washed with $CHCl_3$ (30 mL), acidified (conc HCl with ice), and the resulting solution was extracted with $CHCl_3$ (3 x 30 mL). The organic layer was washed with water (50 mL), dried ($MgSO_4$), and evaporated to dryness to give 0.436 g (86%) of **7a**, mp 203-203.5°C (CH_2Cl_2:hexane) (Lit.[13] mp 200.5-201.5°C); IR (Nujol) ν(max) 1702, 1537 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3-7.7 (m, 7H, ArH), 8.12 (dd, J = 1.5, 7.9 Hz, 1H, ArH); MS m/e (rel intensity) 243 (M, 96), 226 (15), 196 (23), 195 (27), 152 (95), 115 (100).

According to the above procedure, the following compounds were prepared:

2-Carboxy-4-Nitrobiphenyl (7b). 2-Formyl-4-nitrobiphenyl (0.227 g, 1.00 mmol), $KMnO_4$ (0.237 g, 1.50 mmol); yield: 72%; mp 172.5-174°C (CH_2Cl_2:cycloxhexane) (Lit.[14] mp 173°C); IR ($CHCl_3$) ν(max) 3425 (br), 1710, 1524, 1346 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32-7.46 (m, 5H, ArH), 7.58 (d, J = 8.5 Hz, 1H, ArH), 8.38-8.43 (dd, J = 2.4, 8.5 Hz, 1H, ArH), 8.80 (d, J = 2.4 Hz, 1H, ArH); MS m/e (rel intensity) 243 (M, 100), 226 (37), 152 (29).

2-Carboxy-5-Nitrobiphenyl (7c). 2-Formyl-5-nitrobiphenyl (0.109 g, 0.48 mmol), $KMnO_4$ (0.116 g, 0.74 mmol); yield: 98%; mp 180-181°C (CH_2Cl_2:hexane) (Lit.[15] mp 180°C); IR (Nujol) ν(max) 3200, 1688, 1521, 1308 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3-7.5 (m, 5H, ArH), 8.10-8.35 (m, 3H, ArH); MS m/e (rel intensity) 244 (M + 1, 15), 243 (M, 100), 226 (35), 152 (47).

2-Carboxy-2'-Nitrobiphenyl (7d). 2-Formyl-2'-nitrobiphenyl (0.191 g, 0.84 mmol), $KMnO_4$ (0.205 g, 1.29 mmol); yield: 90%; mp 170-170.5°C (CH_2Cl_2:hexane) (Lit.[16] mp 168°C); IR (Nujol) ν(max) 3411, 1690, 1677, 1517, 1345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20-7.25 (m, 2H, ArH), 7.40-7.65 (m, 4H, ArH), 8.05-8.15 (m, 2H, ArH); MS m/e (rel intensity) 243 (M, 1), 197 (100), 152 (18).

Preparation of Nitrofluorenones 8a-c; General Method:

1-Nitrofluorenone (8a). A mixture of 2-carboxy-3-nitrobiphenyl **(7a)** (0.383 g, 1.58 mmol) and polyphosphoric acid (6.126 g, 18.10 mmol) was heated at 160°C for 5 h, cooled to room temp, and poured into a mixture of 10% aq NaOH in ice (50 mL). Standard workup followed by chromatography (PhH) gave 0.221 g (62%) of **8a**, mp 189-189.5°C (CH_2Cl_2:hexane) (Lit.[13] mp 188.5-189.5°C); IR (Nujol) ν(max) 1716, 1532, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.39 (ddd, J = 7.3, 6.3, 2.3 Hz, 1H, ArH), 7.5-7.7 (m, 5H, ArH), 7.76 (dd, J = 7.1, 1.4 Hz, 1H, ArH).

The following compounds were prepared according to the general method given above:

2-Nitrofluorenone (8b). 2-Carboxy-4-nitrobiphenyl (0.153 g, 0.60 mmol), PPA (2.360 g, 7.00 mmol); yield: 66%; mp 222-223°C (CH_2Cl_2:hexane) (Lit.[13] mp 219-220°C); IR ($CHCl_3$) ν(max) 1724, 1528, 1340 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41-7.63 (m, 3H, ArH), 7.77-7.81 (m, 1H, ArH), 7.93-8.05 (m, 1H, ArH).

3-Nitrofluorenone (8c). 2-Carboxy-5-nitrobiphenyl (0.100 g, 0.41 mmol), PPA (1.512 g, 4.47 mmol); yield: 88%; mp 235-235.5°C (CH_2Cl_2:hexane) (Lit.[13] mp 232°C); IR (Nujol) ν(max) 1708, 1527, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43 (ddd, J = 7.1, 7.1, 1.7 Hz, 1H, ArH), 7.55-7.8 (m, 3H, ArH), 7.81 (d, J = 8.0 Hz, 1H, ArH), 8.20 (dd, J = 8.0, 1.9 Hz, 1H, ArH), 8.35 (d, J = 1.9 Hz, 1H, ArH).

4-Nitrofluorenone (8d). 2-Carboxy-2′-nitrobiphenyl (0.165 g, 0.68 mmol), PPA (2.477 g, 7.33 mmol); yield: 77%; mp 174-174.5°C (CH_2Cl_2:hexane) (Lit.[17] mp 172.5-173°C); IR (Nujol) ν(max) 1723, 1521, 1306 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4-7.65 (m, 3H, ArH), 7.79 (dd, J = 7.3, 1.3 Hz, 1H, ArH), 7.95 (dd, J = 7.3, 1.1 Hz, 1H, ArH), 8.00-8.05 (m, 2H, ArH).

Preparation of Hydroxymethyl Nitrobiphenyls 9a-d; General Procedure:

2-Hydroxymethyl-5-Nitrobiphenyl (9c). A solution of 2-bromomethyl-5-nitrobiphenyl (0.747 g, 2.55 mmol and KOAc (0.512 g, 5.22 mmol) in HOAc (10 mL) was refluxed for 4 h, cooled, and treated with water (50 mL). The mixture was extracted with $CHCl_3$ (3 x 50 mL) and the organic layer was successively washed with water (50 mL) and saturated aq $NaHCO_3$ (50 mL), dried ($MgSO_4$), and evaporated to dryness in vacuo. The crude **2-acetoxymethyl-5-nitrobiphenyl** was dissolved in an EtOH (5 mL)-THF (15 mL) mixture, 1N aq NaOH (3.8 mL) was added, and the mixture was stirred at room temp. for 12 h. Standard workup and chromatography (hexane-EtOAc, 4:1 → 3:1) afforded 0.523 g (89%) of **9c**; oil; IR (neat) ν(max) 3401, 1522, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.03 (br, 1H, OH), 4.69 (s, 2H, CH_2), 7.25-7.50 (m, 5H, ArH), 7.79 (d, J = 8.5 Hz, 1H, ArH), 8.11 (d, J = 2.4 Hz, 1H, ArH), 8.21 (dd, J = 2.4, 8.5 Hz, 1H, ArH); MS m/e (rel intensity) 229 (M, 66), 165 (100), 152 (76).

According to the above method, the following compounds were prepared:

2-Hydroxymethyl-3-Nitrobiphenyl (9a). 2-Bromomethyl-3-nitrobiphenyl (0.803 g, 2.75 mmol), KOAc (0.542 g, 5.52 mmol), 1N NaOH (4.2 mL, 4.2 mmol); yield: 87%; mp 66-66°C (Et_2O:hexane); IR (Nujol) ν(max) 3572, 1527, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.05 (br, 1H, OH), 4.57 (s, 2H, CH_2), 7.42-7.54 (m, 6H, ArH), 7.63 (dd, J = 1.3, 7.7 Hz, 1H, ArH), 7.93 (dd, J = 1.3, 8.1 Hz, 1H, ArH); MS m/e (rel intensity) 229 (M, 5), 182 (41), 165 (38), 152 (100).

2-Hydroxymethyl-4-Nitrobiphenyl (9b). 2-Bromomethyl-4-nitrobiphenyl (0.611 g, 2.09 mmol), KOAc (0.415 g, 4.22 mmol), 1N NaOH (3.2 mL, 3.2 mmol); yield: 96%; oil; IR (neat) ν(max) 3395, 1516, 1344 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05 (br, 1H, OH), 4.68 (s, 2H, CH_2), 7.30-7.50 (m, 6H, ArH), 8.17 (dd, J = 2.2, 8.4 Hz, 1H, ArH), 8.48 (d, J = 2.2 Hz, 1H, ArH); MS m/e (rel intensity) 229 (M, 62), 211 (31), 181 (23), 165 (100), 152 (68).

2-Hydroxymethyl-2′-Nitrobiphenyl (9d). 2-Bromomethyl-2′-nitrobiphenyl (0.265 g, 0.91 mmol), KOAc (0.180 g, 1.84 mmol), 1N NaOH (1.4 mL, 1.4 mmol); yield: 95%; mp 84-84.5°C (Et_2O:hexane) (Lit.[12] mp 80-82°C); IR (Nujol) ν(max) 3238, 1520, 1344 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74 (br, 1H, 0H), 4.46 (br, 2H, CH_2), 7.10 (dd, J = 1.0, 7.5 Hz, 1H, ArH), 7.20-7.70 (m, 6H, ArH), 7.99 (dd, J = 1.2, 8.0 Hz, 1H, ArH); MS m/e (rel intensity) 229 (M, 10), 198 (25), 182 (76), 152 (82), 166 (100).

Preparation of Nitrofluorenes 10a-c; General Procedure:

3-Nitrofluorene (10c). A mixture of 5-nitro-2-hydroxymethylbiphenyl (**9c**) (0.088 g, 0.383 mmol) and PPA (1.764 g, 5.2 mmol) in $CHCl_3$ (5 mL) was refluxed for 26 h, cooled, and treated with a slurry of 10% aq NaOH (30 mL) and ice. The whole was extracted with $CHCl_3$ (3 x 40 mL) and subjected to standard workup to give, after chromatography (hexane-EtOAc, 20:1 → 10:1), 0.068 g (84%) of **10c**, mp 105-106°C (CH_2Cl_2:hexane) (Lit.[18] mp 103-106°C). If $CHCl_3$ was omitted, the yield of **10c** was lower (35%); IR (neat) ν(max) 1524, 1338 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.99 (s, 2H, CH_2), 7.35-7.5 (m, 2H, ArH), 7.55-7.6 (m, 1H, ArH), 7.65 (d, J = 8.3 Hz, 1H, ArH), 7.85-7.9 (m, 1H, ArH), 8.18 (dd, J = 8.3, 2.2 Hz, 1H, ArH), 8.58 (d, J = 2.2 Hz, 1H, ArH).

1-Nitrofluorene (10a). 3-Nitro-2-hydroxymethylbiphenyl (0.108 g, 0.47 mmol), PPA (1.444 g, 4.5 mmol); yield: 86% without $CHCl_3$ as solvent; mp 106-106.5°C (CH_2Cl_2:hexane) (Lit.[18] mp 104-106°C); IR (Nujol) ν(max) 1518, 1338 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.39 (s, 2H, CH_2), 7.3-7.65 (m, 4H, ArH), 7.8-7.85 (m, 1H, ArH), 8.06 (d, J = 7.5 Hz, 1H, ArH), 8.16 (d, J = 8.2 Hz, 1H, ArH).

2-Nitrofluorene (10b). 4-Nitro-2-hydroxymethylbiphenyl (0.095 g, 0.41 mmol); PPA (1.394 g, 4.13 mmol); $CHCl_3$ as solvent; yield: 79% (without $CHCl_3$, yield: 55%); mp 154-154.5°C (CH_2Cl_2:hexane) (Lit.[19] mp 156°C); IR (Nujol) ν(max) 1515, 1334 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.01 (s, 2H, CH_2), 7.4-7.45 (m, 2H, ArH), 7.6-7.65 (m, 1H, ArH), 7.8-7.9 (m, 2H, ArH), 8.30 (dd, J = 8.4, 2.0 Hz, 1H, ArH), 8.39 (d, J = 2.0 Hz, 1H, ArH).

4-Nitrofluorene (10d). A solution of **8d** (0.093 g, 0.41 mmol) and triethylsilane (0.142 g, 1.22 mmol) in CF_3COOH (4 mL) was stirred at room temp for 2 d. Standard workup and chromatography (hexane:PhH, 3:1 → 2:1) furnished 0.034 g (39%) of **10d**, mp 76-76.5°C (CH_2Cl_2:hexane) (Lit.[17] mp 75-76°C); IR (Nujol) ν(max) 1521, 1347 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.98 (s, 2H, CH_2), 7.35-7.45 (m, 3H, ArH), 7.55-7.6 (m, 1H, ArH), 7.75 (dd, J = 7.5, 0.9 Hz, 1H, ArH), 7.86 (d, J = 8.0 Hz, 1H, ArH), 8.0-8.1 (m, 1H, ArH).

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7. Of the other isomers, **8a** yielded a mixture, **8b** gave starting material (32%) and carbinol **i** (64.5%), and **8c** afforded nitrofluorene **10c** (14%) and carbinol **i** (73%). Further reduction of the 1- and 3-nitro carbinols **i** under the Et_3SiH or $NaBH_4$/THF (Gribble, G., Kelly, W., Emery, S. Synthesis, **1978**, 763) conditions gave starting material and dimer **ii**. Reduction of 1-nitroflurenone ($(Et_3SiH/TiCl_4)$ gave carbinol **i** and the dimer **iii**.